Message

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Sent: 6/14/2019 8:52:02 PM
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Subject: STICS: Clearance Completion: #ORD-015704: Linking a dermal permeation and an inhalation model to a simple pharmacokinetic model to study airborne exposure to di(n-butyl) phthalate

The clearance for this Human Health Risk Assessment product is complete:

- **Product type, subtype:** Journal Article, Peer Reviewed
- **Product title:** Linking a dermal permeation and an inhalation model to a simple pharmacokinetic model to study airborne exposure to di(n-butyl) phthalate
- **Author(s):** Lorber, M,C. Weschler,G. Morrison and G. Beko
- **Initiator:** Matthew Lorber,ord/ncea/nceawa/qrmg
- **ORD Tracking Number:** Tracking # ORD-015704
- **Impact / Purpose Statement:** This journal article collaboration between an EPA primary author and authors external to EPA is a modeling study which predicts body burdens and exposures to airborne phthalates. It will provide insights into the relative importance of these pathways (mainly inhalation and dermal penetration) compared to overall phthalate exposure.
- **Product Description / Abstract:** Six males clad only in shorts were exposed to high levels of airborne di(n-butyl) phthalate (DnBP) and diethyl phthalate (DEP) in chamber experiments conducted in 2014. In two 6-hr sessions, the subjects were exposed only dermally while breathing clean air from a hood, and both dermally and via inhalation when exposed without the hood. Full urine samples were taken before, during, and for 48 hours after leaving the chamber and measured for key DnBP and DEP metabolites. The data clearly demonstrated high levels of metabolite excretions while in the chamber and during the first 24 hours once leaving the chamber under both conditions. The data for DnBP were used in a modeling exercise linking dose models for inhalation and transdermal permeation with a simple pharmacokinetic model which predicted timing and mass of metabolite excretions. These models were developed and calibrated independent of these experiments. Tests included modeling of the "hood-on" (transdermal penetration only), "hood-off" (both inhalation and transdermal) scenarios, and an "inhalation-only" scenario. Results showed that the linked model tended to duplicate the pattern of excretion with regard to timing of peaks, decline of concentrations over time, and the ratio of DnBP metabolites. However, the transdermal model tended to overpredict penetration of DnBP such that predictions of metabolite excretions were between 1.2 and 4.5 times higher than the cumulative excretion of DnBP metabolites over the 54 hours of the simulation. A similar overprediction was not seen for the "inhalation-only" simulations. Possible explanations and model refinements for these overpredictions are discussed. In a demonstration of the linked model designed to characterize general population exposures to typical airborne indoor concentrations of DnBP in the United States, it was estimated that up to one-quarter of total exposures could be due to inhalation and dermal uptake.
- **Tracking and Planning**
  - Task ID: HHRA333
  - Task: Cumulative Risk Assessment and Resources
  - Product Title: N/A - Not Applicable
  - Product Description: N/A - Not Applicable
  - Project: Cumulative Risk Methods and Impact Assessments
  - Topic:

- Research Program Area: Human Health Risk Assessment

- **Product Category:** Does not require Advance Notification
- **QA form attached in STICS?:** Not Applicable
- **QAPP Reference:** N/A
- **Keywords:**
  - Cumulative Exposure
  - Phthalates
  - Dermal Exposure
  - Di(n-butyl) phthalate

- **Journal Name:** Journal of Exposure Science and Environmental Epidemiology
- **DOI:** https://doi.org/10.1038/jes.2016.48
- **Published Date:** 11/01/2017

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